

THE CANADIAN MEDICAL ASSOCIATION
LE JOURNAL DE
L'ASSOCIATION MÉDICALE CANADIENNE

AUGUST 14, 1965 • VOL. 93, NO. 7

The Significance of Regional Lymph Node Metastases in
Breast Carcinoma

JAMES E. DEVITT, M.D., C.M., M.Sc., F.R.C.S.(Edin.), F.R.C.S.[C],
Ottawa, Ont.

ABSTRACT

The significance traditionally attached to regional lymph node metastases has been questioned following a retrospective review of 922 patients with early breast cancer.

Conservative surgical removal of axillary lymph node metastases and conservative irradiation of internal mammary lymph node metastases did not prejudice the five- and 10-year survival rates of patients so treated.

Axillary lymph node recurrences had an ominous prognosis and occurred more commonly in the conservatively treated patients, yet survival rates were the same as those following radical mastectomy. Many axillary lymph node recurrences occurred more than five years after primary therapy, or with or after other evidence of reactivation of the breast cancer.

It is suggested that breast cancer patients do not do poorly because they have regional lymph node metastases, but rather they have these metastases when they do poorly.

SOMMAIRE

L'auteur, après un étude rétrospective portant sur 922 cas de cancer mammaire au début, met en doute le rôle attribué aux métastases ganglionnaires régionales.

L'exérèse chirurgicale conservatrice des métastases aux ganglions axillaires et l'irradiation conservatrice des métastases aux ganglions mammaires internes, n'ont pas modifié les survies de cinq et 10 ans chez les malades ayant reçu ces traitements.

Les cas de récurrence aux ganglions axillaires ont eu un pronostic inquiétant et se sont produites plus souvent chez les malades soumis à un traitement conservateur, encore que les taux de survie aient été les mêmes que chez ceux des malades qui avaient subi une mammectomie radicale. De nombreuses récurrences axillaires sont survenues plus de cinq ans après le traitement initial ou accompagnaient ou suivaient d'autres signes de réactivation du cancer mammaire.

On estime que les malades qui ont eu une néoplasie mammaire ne dépérissent pas parce qu'il ont des métastases ganglionnaires régionales, mais au contraire qu'ils ont ces métastases parce qu'ils dépérissent.

THE belief in the importance of regional lymph node metastases in the spread of carcinoma is very deeply rooted in medical lore. This concept is used to justify the treating, whether by surgery or irradiation, of the regional lymph nodes that drain an organ bearing a carcinoma. It is difficult, however, to reconcile this belief with five obser-

ventions made on the 922 patients with "curable" breast cancer, seen in the Civic Hospital Division, Ottawa Clinic of the Ontario Cancer Foundation, who first received treatment in the years 1946 to 1959. At the outset it must be clearly understood that these observations were made on the basis of a retrospective review,¹ and that no planned random distribution of patients into the different treatment groups was undertaken.

From the Division of Surgery, Ottawa Civic Hospital, and the Civic Hospital Division, Ottawa Clinic, Ontario Cancer Foundation.

Presented at the 34th Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Toronto, January 1965.

OBSERVATION 1:

Concerning Axillary Lymph Node Metastases

If axillary lymph node metastases of a breast cancer are important sources of further spread, it would seem likely that their radical removal would be attended by better survival rates than those associated with methods which leave these nodes in place. As well, it would be expected that patients with axillary metastases undergoing radical mastectomy would have better survival rates than those having only a simple mastectomy with conservative or accidental removal of those axillary contents adjacent to the axillary tail of the breast.

TABLE I.—CRUDE SURVIVAL RATES FOR PATIENTS WITH STAGE II LESIONS

	5-year (1946-1959)	10-year (1946-1954)
Radical mastectomy patients . . .	48% (243)	24% (158)
Conservative surgery patients . . .	52% (62)	50% (26)

(Figures in parentheses indicate the number of patients at risk.)

Retrospective review of 305 patients with *histologically* proved axillary lymph node metastases showed that the radical mastectomy patients did not do better than those subjected to simple mastectomy. Considering only those patients with a pathological diagnosis of lymph node metastases, it is seen in Table I that the five-year survival rate of the 243 radical mastectomy patients was 48%, compared to a five-year survival rate of 52% for the 62 patients treated by simple mastectomy and lower axillary excision. After 10 years—that is, in the patients first treated between 1946 and 1954—only 24% of the 158 radical mastectomy patients were alive, while 50% of the 26 simple mastectomy patients survived.

Fig. 1 shows the year-by-year survival rates for the two groups of patients. Again, it is seen that the radical excision of the axillary contents did not improve the survival rates of the patients so treated. The irregularities of the simple mastectomy curve after the sixth year are due, of course, to the small number of patients in the study.

These findings cannot be explained by any obvious prejudicial selection of patients.¹ The retrospective assigning of the primary tumours in the two groups into stages T₁ and T₂ by the author revealed the proportions to be identical in each group. The surgeons concerned were in the habit of doing either radical mastectomy routinely or simple mastectomy routinely. None performed radical mastectomy on clinical Stage II patients and simple mastectomy on those with Stage I lesions. Rather, because of the limited lymph node removal, it is possible that metastases would only be found in those conservatively treated patients

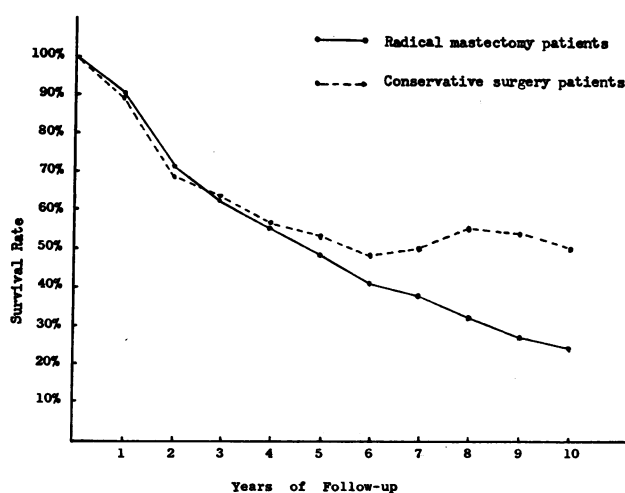


Fig. 1.—Crude year-by-year survival rates of patients with Stage II breast carcinoma.

with the more extensive involvement. Thus the simple mastectomy patients may have had, as a group, more advanced malignant disease, there being less opportunity for the finding of chance microscopic deposits in this group. The conservatively treated patients were older (Fig. 2), but this should have lowered their crude survival rates,² particularly at the 10-year follow-up.³ Seventeen of the radical mastectomy patients and two of the simple mastectomy patients did not receive routine prophylactic radiotherapy.

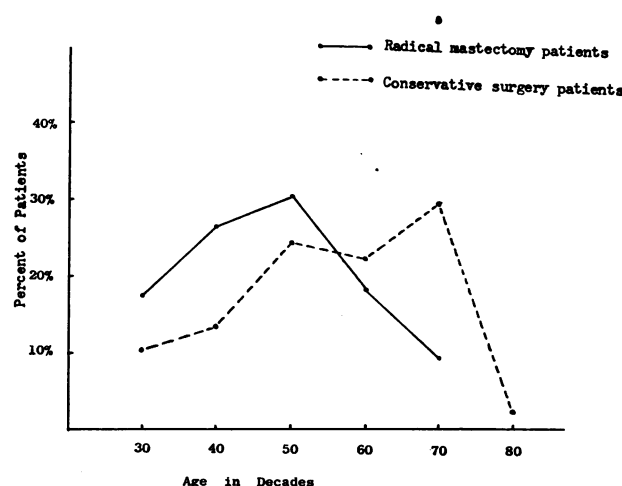


Fig. 2.—Age distribution of patients with Stage II breast carcinoma.

The failure of radical axillary dissection to improve survival rates has been previously observed in a clinical trial in Copenhagen,^{4, 5} where simple mastectomy with postoperative irradiation was compared to the extended radical mastectomy, and in Cambridge⁶ where the results obtained with modified simple mastectomy and postoperative irradiation are being compared to radical mastectomy and postoperative irradiation. The ineffectiveness of radical axillary adenectomy has been most dramatically demonstrated by Porritt,⁷ who has favour-

ably compared segmental mastectomy and axillary biopsy to radical mastectomy, both being followed with irradiation.

Does not the failure of the radical removal of the axillary metastases to improve survival rates suggest that these regional lymph node metastases may not be responsible for further spread of the cancer?

OBSERVATION 2:

Concerning Internal Mammary Lymph Node Metastases

If the internal mammary lymph node metastases of a breast cancer are important sources of further spread, it would be expected that the survival rates for patients with medial-half primary lesions should be poorer than those with primary tumours in the lateral half of the breast, since it is well accepted that the former have a higher incidence of internal mammary metastases. None of the patients in this study were subjected to the operation of extended radical mastectomy, and prior to mid-1953 none had irradiation of the internal mammary chains.

TABLE II.—CRUDE SURVIVAL RATES FOR PATIENTS WITH "CURABLE" BREAST CARCINOMA ACCORDING TO LOCATION

	5-year (1946-1959)	10-year (1946-1954)
Medial-half lesions	65% (228)	48% (150)
Lateral-half lesions	65% (525)	43% (313)

(Figures in parentheses indicate the number of patients at risk.)

In Table II the five-year and 10-year survival rates are shown for those patients whose primary tumours were described as being in the lateral and the medial halves of the breast (excluded are 97 patients with central tumours and 72 in whom the exact location was not recorded). It is seen that the failure to remove the internal mammary lymph nodes in any, and the failure to irradiate these nodes in half of the patients, did not prejudice the survival of those who had medial-half lesions, with their associated greater incidence of internal mammary metastases. In other words, although the patients with medial-half lesions should have had a greater number of untreated (by surgery or radiotherapy) internal mammary lymph node metastases, their survival rates were the same as those patients with lateral-half lesions. Similarly, MacKay and Sellers,² in a review of over 11,000 patients, did not observe a poorer prognosis for patients with lesions in the medial portion of the breast.

This second observation tends to refute the argument that radiotherapy, which was given to most patients, will have destroyed any retained, involved lymph nodes. Full refutation of this argument is perhaps provided by the few properly conducted randomized clinical trials that have been reported.

At Manchester^{8,9} the prophylactic postoperative irradiation of radical mastectomy patients did not improve survival rates over the rates of those who did not receive radiotherapy. Thus irradiation of the internal mammary and supraclavicular lymph node metastases did not improve survival. Are the axillary lymph node metastases likely to behave differently from those in the internal mammary and supraclavicular nodes? At Copenhagen,^{4,5} where patients subjected to extended radical mastectomy had survival rates equal to those following simple mastectomy with radiotherapy, it was concluded that irradiation and surgical removal were equally effective (or ineffective¹⁰) in dealing with the regional lymph node metastases, or perhaps the regional lymph node metastases are not important in determining survival. It would seem, then, that since treating the regional lymph node metastases does not appear to improve survival rates, these metastases may not be important in themselves in determining survival. Presumably they are not important sources of further spread.

OBSERVATION 3:

Concerning the Incidence of Axillary Lymph Node Recurrence

The significance of regional lymph node metastases was studied further by reviewing the homolateral axillary lymph node recurrences. As a rule these were clinical rather than pathological diagnoses. Table III shows the incidence of these re-

TABLE III.—HOMOLATERAL AXILLARY LYMPH NODE RECURRENCES DEVELOPING WITHIN FIVE YEARS IN PATIENTS WITH STAGE I AND STAGE II BREAST TUMOURS

No. of patients	No. of recurrences
549 Radical mastectomy + x-ray	7
51 Radical mastectomy alone	3 { 65% five-year survival rate; 46% 10-year survival rate
5 X-ray + radical mastectomy	0
605 Total radical group	10 (1.7%)
260 Simple mastectomy + x-ray	14
36 Simple mastectomy alone	6
7 X-ray + simple mastectomy	1 { 66% five-year survival rate; 47% 10-year survival rate
14 Tumour excision ± x-ray	1
317 Total conservative group	22 (6.9%)

currences in the combined Stage I and Stage II patients. It was significantly higher in those who had conservative surgery, being 6.9% in the first five years, whereas only 1.7% of the radical mastectomy patients developed axillary recurrences. Moreover, of the 14 patients who developed axillary recurrences after five years, 12 had had conservative surgery (Table IV). Most of the patients who developed axillary recurrences have died of breast cancer. Yet, in spite of this ominous prognosis, and in spite of the higher incidence of axillary lymph node recurrences, the crude survival rates for all

TABLE IV.—HOMOLATERAL AXILLARY LYMPH NODE RECURRENCES DEVELOPING AFTER FIVE YEARS

<i>Year of appearance after primary treatment</i>	<i>No. of recurrences</i>	<i>Treatment of primary lesions</i>	
6th	2	Radical mastectomy + x-ray..	1
7th	3	Radical mastectomy alone....	1
8th	6	Simple mastectomy + x-ray...	3
9th	2	Simple mastectomy alone.....	6
10th	1	X-ray + simple mastectomy...	1
		Tumour excision + x-ray.....	1
		Tumour excision alone.....	1

conservatively treated patients were the same as those for women who had had radical mastectomy. If these axillary lymph node recurrences were significant sources for further spread of the cancer, it might have been expected that the simple mastectomy patients would have had worse survival rates, by reason of the difference in the incidence of recurrence.

OBSERVATION 4:

Concerning Late Axillary Lymph Node Recurrences

By the end of 1964, 14 patients had developed homolateral axillary lymph node recurrences more than five years after the primary therapy (Table IV). Some of the patients treated between 1955 and 1959 will presumably still develop axillary recurrences before they reach their 10-year follow-up. It can be seen that two of the recurrences appeared in the 6th year, three in the 7th year, six in the 8th year, two in the 9th year, and one in the 10th year after treatment. Crile¹¹ has reported similar observations on axillary lymph node recurrences and Sanger¹² on internal mammary lymph node recurrences. These lymph node metastases must have been present all of the time. Thus it would appear that regional lymph node metastases can either grow very slowly or, more likely, that they may remain quiescent for many years in peaceful co-existence with their host.

OBSERVATION 5:

Concerning the Timing of Axillary Lymph Node Recurrences

Table V shows the relative timing of all of the axillary lymph node recurrences. In 19 of the patients these recurrences represented the first sign of

TABLE V.—RELATIVE TIMING OF AXILLARY LYMPH NODE RECURRENCES

First recurrence.....	19	
Simultaneous with skin recurrence.....	4	
Simultaneous with supraclavicular nodes.....	3	
After repeated skin recurrence.....	5	
		12
Simultaneous with distant metastases.....	9	
After distant metastases.....	6	
		15

reactivation of the disease. In 12 they appeared simultaneously with or after other local evidence of reactivation of the cancer. In the remaining 15 they appeared simultaneously with or after distant metastases. Thus axillary lymph node recurrences do not necessarily precede the appearance of the disease elsewhere, which they should if the nodes were important sources of further spread.

DISCUSSION

Retrospective reviews such as that presented in this communication will never do more than suggest the probable result of a properly randomized prospective study. However, these five observations are not readily reconciled with the concept that the regional lymph nodes are important way-stations in the spread of breast cancer. This, of course, is not to suggest that a primary tumour which has the biological aggressiveness to produce regional lymphatic metastases does not have a poorer outlook than a primary tumour that has not produced such metastases. But possibly the lymph node metastases are only the expression of basic biological factors, and not the cause of the poor outlook.^{13, 14} Perhaps the regional lymph node metastases are in themselves unimportant local accidents, reflecting only the likelihood that the host's "resistance" has broken down elsewhere.

SUMMARY

Five observations concerning regional lymph node metastases have been made on 922 retrospectively reviewed patients with "curable" breast cancer.

1. In patients with histologically proved axillary metastases, similar survival rates were achieved by means of radical mastectomy, and simple mastectomy with conservative or accidental removal of the adjacent axillary contents.

2. Patients with tumours in the medial half of the breast, and therefore presumably a higher incidence of untreated internal mammary lymph node metastases, had survival rates equal to those with lateral half lesions.

3. The higher incidence of axillary lymph node recurrences, with their ominous prognosis, did not appear to influence the survival rates of those patients treated by conservative surgery.

4. Fourteen of the 46 axillary lymph node recurrences appeared more than five years after the original treatment.

5. Axillary lymph node recurrences frequently appeared with or after other evidence of reactivation of the breast cancer.

It is suggested that the poor prognosis associated with metastatic regional lymph nodes is not due to these metastases. Rather, both prognosis and metastases are evidence of the biological activity of the tumour. The possibility is considered that the metastases in regional lymph nodes may not be important sources for further spread of breast cancer.

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Sarcoidosis and Polyarthrititis

L. M. ANHOLT, M.D., SQUADRON LEADER, R.C.A.F. and
RICHARD H. ROBERTS, M.D., F.A.C.P., SURGEON CAPTAIN, R.C.N.,
Halifax, N.S.

ABSTRACT

Polyarthrititis is a well-recognized manifestation of sarcoidosis, but the various series of cases reported in the literature reveal considerable variation in its incidence as well as in its clinical manifestations. Three major types of sarcoid polyarthrititis are defined, as distinguished by their clinical and pathological features. Two of these types are usually seen in conjunction with the subacute or transient form of sarcoidosis and, in most cases, are accompanied by erythema nodosum. They differ markedly in severity, but their prognosis is uniformly good. The third type, in contrast, is of a chronic nature and is often associated with permanent joint changes. Mild joint manifestations are a frequent finding in sarcoidosis, but more severe arthritis is relatively rare.

Two cases of sarcoidosis, presenting with severe polyarthrititis, are reported in detail, and cases seen in Halifax hospitals during the period 1954 to 1964 are reviewed.

SOMMAIRE

La polyarthrite est une manifestation bien connue de la sarcoïdose, mais les divers groupes de cas qui ont été publiés dans la littérature médicale indiquent qu'il y a de fortes variations dans sa fréquence ainsi que dans ses manifestations cliniques. On définit trois types principaux de polyarthrite sarcoïdienne selon leurs caractéristiques cliniques et pathologiques. Deux de ces formes s'observent généralement concurremment avec la forme subaiguë ou transitoire de la sarcoïdose et, dans la plupart des cas, s'accompagnent d'érythème noueux. Leurs degrés de gravité diffèrent grandement, mais leur pronostic est toujours bon. Par contre, le troisième type est de caractère chronique et s'accompagne souvent de modifications articulaires permanentes. Les manifestations articulaires bénignes sont une observation fréquente de la sarcoïdose, mais l'arthrite de forme plus grave est relativement rare.

L'auteur rapporte en détail deux cas de sarcoïdose avec polyarthrite grave et passe en revue les cas qui ont été observés dans les hôpitaux de Halifax pendant la période de 1954 à 1964.

SINCE 1899 when Boeck¹ first described the clinical and pathological findings and named the syndrome "sarcoidosis", an increasing number of reports concerning this disorder have appeared in the literature each year. Although joint involvement was first described by Burman and Mayer² in 1936, this aspect of the disease at first attracted little attention. This communication will describe in detail two cases seen at the Canadian Forces Hos-

pital, Halifax, in 1963,³ will discuss the cases treated in other Halifax hospitals during the period 1954 to 1964, and will briefly review the literature on the subject.

CASE REPORTS

CASE 1

A 27-year-old white Air Force corporal was admitted to the Canadian Forces Hospital, Halifax, with a history of a swollen, red, painful left foot of six days'

From the Department of Medicine, Dalhousie University, and the Canadian Forces Hospital, Halifax, Nova Scotia. Presented at the 34th Annual Meeting of the Royal College of Physicians and Surgeons of Canada, Toronto, January 1965. The case reports presented in this article are reproduced by permission of the *Medical Services Journal, Canada*.